America's Blood Centers

It's About *Life*.

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Rockville, Maryland 20852

Re: Docket No. 2004N-0539: Development of Plasma Standards Public Workshop

Dear Docket Officer:

America's Blood Centers (ABC) appreciates this opportunity to provide additional public comments on the Food and Drug Administration's (FDA) public workshop "Development of Plasma Standards (the Workshop) on August 31 and September 1, 2004.

For your information, ABC member centers supply about half of the nation's blood and blood components for transfusion. Plasma separated from Whole Blood is processed into Fresh Frozen Plasma (FFP) or shipped for further manufacturer into plasma derivatives. About 25 percent of available plasma from ABC centers is used for the latter purpose.

We have the following comments:

1. **ABC supports the goal of harmonization of regulations for collection, freezing, and storage of plasma but urges that it be based on science-based standards.**

   Comments at the workshop from the user community focused on safety and availability. If all blood collection facilities prepare plasma products the same way, when they are shipped to the manufacturers worldwide, the manufacturers can treat them in the same way and have a reliable end product at the end of the manufacturing process.

2. **The goal of any changes in regulation ultimately should be safe and effective products for patients worldwide.**

   Data presented by several speakers at the Workshop showed that there is very little difference in Factor VIII concentrate end products from different source materials. In general, plasma for transfusion is not used to replace labile components. Appropriate factor concentrates and recombinant factors are used for that purpose.

   More importantly, there is no scientific reason why Factor VIII should drive standards. The plasma derivative manufacturers specify the requirements for their raw materials according to their validated procedures. They will select the best available product to fulfill their needs.

3. ABC urges FDA to consider the best use of resources to produce safe and effective plasma products.

Instead of implementing regulations that would require changes in storage temperatures, replacing freezers, and going to dual-cascade systems that are costly, require much more maintenance and are more trouble-prone, resources might be better applied to answering questions about the impact of a change in source material on the end plasma product. For example, an important question is the impact, if any, of storage and transport conditions on inhibitor formation.

From a biological standpoint, the rate of freezing is very important in preserving both cells and proteins. So we believe that defining the rate is important. But we urge FDA to consider the impact on supply of making the freezing rate too restrictive in a fairly robust system. Data presented at the Workshop demonstrated that current processes produce factor concentrates and other derivatives of high yield and activity.

4. We recommend that additional specifications be left to the manufacturers.

The plasma derivative manufacturers have taken years to develop their procedures, optimize their production, validate their processes, and go through a very rigorous review by FDA not only for their processes, but their final products.

ABC believes that the manufacturers must define the collection, freezing, and storage conditions of the raw materials they choose according to their final product and validation requirements. The creation of a standard raw material could restrict supply, impacting products that are not labile protein dependent, such as IGIV.

5. ABC supports FDA's intent to develop standards for that would allow licensure of Recovered Plasma

Recovered plasma is the only product for interstate commerce that is not licensed, does not require FDA approvals prior to manufacture or shipment. It is regulated through short supply agreements between the supplier and the manufacturer, and essentially, each manufacturer or broker who accepts recovered plasma sets their own specifications through the agreements.

For reasons are not entirely clear, current FDA regulations were based on intent of collection. If plasma is collected for further manufacture, it is to be treated one way; if it is collected as whole blood or from an apheresis machine, it is to be used another way.

More recently, FDA has been more flexible and allowed the conversion of fresh frozen plasma to plasma for manufacture prior to its outdating. However, plasma that is collected during apheresis procedures for platelets or for red cells is treated differently and cannot be shipped for further manufacture.

FDA made an exception when blood centers held plasma inventories because of West Nile virus in 2003, and again FDA provided a variance. What this represents, however, is looking for loopholes and "workarounds" to address outdated regulations – instead of updating the regulations, themselves.

ABC requests that the regulations be amended to allow concurrent plasma and all plasma suitable for transfusion to be used for further manufacturer within the parameters specified.

6. ABC fully supports AABB's proposal for Licensing Recovered Plasma.

ABC was involved in the development of the AABB proposal and we believe that it is a simplified proposal that would make the product a recognized product, not an orphan. ABC believes that plasma that is suitable for transfusion into a patient is suitable for further manufacture.

7. The regulations should distinguish recovered plasma from source plasma by frequency of donation, not by end use.

ABC recommends that the distinction made in the regulations between plasma collected by apheresis and plasma separated fro whole blood be made not in terms of the intent of the donation, but in terms of donor protection. In other words, if the volunteer blood organizations collect a unit of plasma several times a week from volunteer plasma donors, they should be subject to all the source plasma regulations.

Thank you for the opportunity to comment.

Yours truly,

G. Michael Fitzpatrick

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America's Blood Centers